



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,995	09/29/2000	Ravi V. J. Chari	104322.198 US1	2588

23373 7590 05/23/2005

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER

CANELLA, KAREN A

ART UNIT PAPER NUMBER

1642

DATE MAILED: 05/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/671,995

Applicant(s)

CHARI, RAVI V. J.

Examiner

Karen A. Canella

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 93-120 and 144-151 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 93-120 and 144-151 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>Oct 12, 2004</u> | 6) <input type="checkbox"/> Other: ____ |

PD

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 14, 2005 has been entered.
2. Claims 144, 146, 148 and 150 have been amended. Claims 93-120 and 144-151 are pending and under consideration.
3. Sections of Title 35, U.S. Code not found in this action can be found in a previous Office action.
4. The rejection of claim 120 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn after reconsideration in light of applicant's arguments. Applicant maintains that "unexpectedly superior results" is synonymous with synergistic. The examiner previously maintained that superior result could be attained by the additive effect of each chemotherapeutic agent or the administration of an agent and an immunoconjugate which obliterates some of the toxic effect of the agent or immunoconjugate which would be in contrast to a synergist effect which would be more than the additive effect of the chemotherapeutic agent and the immunoconjugate. The art recognizes clinical synergism which would be made up of synergism of beneficial actions and toxic effects which would correspond to the "unexpectedly superior results" described in the specification.
5. The rejection of claims 93-97, 99, 102-110, 112, 115-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegall et al (Proc Annu Meet Am Assoc Cancer Res, 1997, Vol. 38, page A185) in view of Chari et al (Cancer Research, 1992, Vol. 52, pp. 127-131) is withdrawn. Applicant argues that Chari et al teach against the claimed invention, but that argument is based on the examiners mis-interpretation of the Chari reference, which will be clarified in the rejections below. However, applicant also argues that there is no reasonable

Art Unit: 1642

expectation of success for the combination of the two references due to the complexity of the interaction between the maytansinoid-immunoconjugate with the cellular machinery and the interaction between paclitaxel and the cellular machinery. This has been considered and found persuasive. The combination of a maytansinoid immunoconjugate and paclitaxel is found to be novel and non-obvious. The search was extended to docetaxel, epothilone A, B, C, D, E, F, and the claims as drawn to these species were also found to be novel and unobvious. The species of cisplatin and etoposide are currently under examination.

6. Claims 93-97, 102-110, 115-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lidor et al (Journal of Clinical Investigation, 1993, Vol. 92, pp. 2440-2447) or Rosenblum et al (Cancer Immunol Immunother, 1996, Vol. 42, pp. 115-121) in view of Chari et al (Cancer Research, 1992, Vol. 52, pp. 127-131, cited in a previous action).

Claim 93 is drawn to a pharmaceutical composition comprising a therapeutically effective amount of at least one chemotherapeutic agent and at least one immunoconjugate; wherein the immunoconjugate comprises at least one maytansinoid compound linked to a monoclonal antibody or fragment thereof and wherein the monoclonal antibody or fragment thereof bind to an antigen expressed by a cancer cell. Claims 94-97 embody the composition of claim 93, wherein the chemotherapeutic agent is cisplatin. Claims 102-104 specify the structure of a modified maytansinoid having a "thiol handle" for conjugation to an antibody.

Claim 106 is drawn to a kit comprising a therapeutically effective amount of at least one chemotherapeutic agent and at least one immunoconjugate; wherein the immunoconjugate comprises at least one maytansinoid compound linked to a monoclonal antibody or fragment thereof and wherein the monoclonal antibody or fragment thereof bind to an antigen expressed by a cancer cell. Claims 107-110 embody the kit of claim 106 wherein the chemotherapeutic agent is cisplatin. Claims 115-117 specify the structure of the maytansinoid having a "thiol handle" for conjugation to an antibody. Claim 118 and 119 specify that the kit of claim 106 comprises the immunoconjugate and chemotherapeutic agent are in the form of separate compositions, and compositions within the kit, respectively. Claim 120 is drawn to a kit comprising a synergistic combination of at least one chemotherapeutic agent which is a platinum

Art Unit: 1642

compound and at least one maytansinoid-immunoconjugate wherein the antibody of the immunotoxin is monoclonal and binds to an antigen expressed by a cancer cell.

Lidor et al teach a supra-additive cytotoxicity afforded by the combination of an immunotoxin and cisplatin (page 2443, first column, bridging sentence to second column). Lidor et al teach that immunotoxins modulate the sensitivity of ovarian cancer cells to alkylators and that the toxicity produced by immunotoxins operates by a mechanism which is distinct from alkylating agents, and thus the combination is advantageous for reasons of imparting to the cancerous cells two separate toxins (page 2446, first column, lines 32-40). Lidor et al teach that the toxin portion of the immunotoxin was ricin A chain (page 2440, first column, lines 11-12 under the heading of "Drugs and Immunoconjugates" and reference 9). Lidor et al do not teach the combination comprising maytansinoid as the toxic portion of the immunoconjugate.

Rosenblum et al teach that 5-FU, cisplatin, interferons alpha and gamma and etoposide augmented the cytotoxicity of an immunotoxin comprising gelonin and an anti gp-240 antibody which binds to a surface glycoprotein on melanoma cells (page 115, first column, lines 3-6, and page 120, first column, lines 7-9, figure 9 and legend for figure 9). Rosenblum et al do not teach the combination comprising maytansinoid as the toxic portion of the immunoconjugate.

Chari et al teach the chemical synthesis of the structures of claims 102-105, 115-117 and 120. Chari et al teach the conjugation of an antibody which specifically binds to the neu antigen on tumor cells, TA.1 (page 128, first column, lines 17-22, Figure 2, page 129, figure 3). Chari et al teach the advantage of using protein toxins versus anticancer drugs in immunoconjugates lies in the fact that protein toxins act catalytically rather than stoichiometrically (page 127, first column, lines 16-22 under the heading of "Introduction"). Chari et al teach that a method of overcoming this difficulty with anticancer drugs is to replace the current anticancer drugs with compounds which have 100 to 1000-fold higher cytotoxicity and conjugate these drugs to antibodies via a disulfide linkage which can be cleaved inside the cell to release the active drug (page 127, first column, lines 32-37 under the heading of "Introduction"). Chari et al identify maytansine as such a drug having 100 to 1000-fold higher toxicity in a range of human cancer cell lines (page 128, first column, first paragraph under "Results and Discussion"). Chari et al teach that the high specific activity of maytansinoid conjugate toward tumor cell lines in comparison with low systemic toxicity indicates that these

Art Unit: 1642

potent conjugates may possess a therapeutic index sufficient for the effective treatment of human cancer (page 130, first column, lines 5-9).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute maytansinoid for the ricin A chain immunoconjugate in the combination of immunotoxin and cisplatin taught by Lidor et al or to substitute maytansinoid for the gelonin of the immunoconjugate taught by Rosenblum et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Chari et al on the high therapeutic index afforded by the use of a maytansinoid immunoconjugate versus ricin A chain because the disulfide linkers provided by Chari et al for the maytansinoid immunoconjugates would be efficient at releasing the toxic maytansinoid for the antibody once internalized by the cell. One of skill in the art would expect that the maytansinoid immunotoxin would have a similar therapeutic potential as the ricin A immunotoxin of Lidor et al or of gelonin in the immunoconjugate taught by Rosenblum et al.

7. Claims 93-97, 99, 102-110, 112, 115-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lidor et al and Chari et al or Rosenblum et al and Chari et al as applied to claims 93-97, 102-110, 115-120 above, and further in view of Schlom (Monoclonal Antibodies: They're More and Less Than You Think, In: Molecular Foundations of Oncology, 1991, Ed. S. Broder, pp. 95-134, cited in s previous Office action).

Claim 99 embodies the composition of claim 93 wherein the monoclonal antibody or fragment thereof is at least one of Fv, Fab, Fab' or F(ab')₂. Claim 112 embodies the kit of claim 106 wherein the monoclonal antibody or fragment thereof is at least one of Fv, Fab, Fab' or F(ab')₂.

The combination of references do not specifically teach immunotoxins wherein the antigen-binding portion is Fv, Fab, Fab' or F(ab')₂.

Schlom teaches the advantages of antibody fragments such as Fab'₂, Fab or Fv over the parent marine antibodies comprise rapid clearance from the blood and body to avoid unwanted by-stander tissue toxicity, reduced accumulation in the kidneys, especially for the avoidance of renal toxicity associated with drug conjugated antibodies, increased penetration of tumor masses, reduced immunogenicity due to lack of antibody effector domains (page 97, second column, line

Art Unit: 1642

22 to page 98, second column, line 5 and page 122, second column, lines 2-23) as well as relative ease of production (lines 27-30).

It would have been prima facie obvious at the time the claimed invention was made to substitute the antigen-binding fragment, such as Fab², Fab or Fv, in place of the whole antibodies in the immunoconjugate taught by Lidor et al or Rosenblum et al. One of skill in the art would have been motivated to do so by the teachings of Schlom on the improved efficacies afforded by the administration of antibody fragments versus whole antibodies.

8. Claims 93-97, 99, 101-110, 112 and 114-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lidor et al and Chari et al or Rosenblum et al and Chari et al as applied to claims 93-97, 102-110, 115-120 above, and further in view of Liu (Expert Opinion on Investigational Drugs, 1997, Vol. 6, pp. 169-172, cited in a previous Office action) and the abstract of Fiorentino et al (Dev Oncol, 1988, Vol. 54, pp. 415-435) and (Schlom, Monoclonal Antibodies: They're More and Less Than You Think, In: Molecular Foundations of Oncology, 1991, Ed. S. Broder, pp. 95-134)

Claim 101 embodies the pharmaceutical composition of claim 93 wherein the monoclonal antibody or fragment thereof is humanized C242. Claim 114 embodies the kit of claim 106 wherein the monoclonal antibody or fragment thereof is humanized C242. Claim 144 is drawn to a pharmaceutical composition comprising paclitaxel and a humanized monoclonal antibody selected from the group consisting of N901 and C242. Claim 146 is drawn to a kit comprising a therapeutically effective amount of paclitaxel and a humanized monoclonal antibody selected from the group consisting of N901 and C242. Claim 148 is drawn to a pharmaceutical composition comprising paclitaxel and a humanized monoclonal antibody or a fragment thereof that binds to an antigen expressed by small cell lung cancer, a non-small cell lung cancer or a colorectal cell. Claim 150 is drawn to a kit comprising a therapeutically effective amount of cisplatin and a humanized monoclonal antibody or a fragment thereof that binds to an antigen expressed by small cell lung cancer, a non-small cell lung cancer or a colorectal cell.

The combinations of Lidor et al and Chari et al or Rosenblum et al and Chari et al do not specifically teach the combination of a humanized C242-DM1 conjugate. However, Lidor et al

Art Unit: 1642

suggest the general property of synergism between an immunotoxin and cisplatin because Lidor et al proposes that the immunotoxin would decrease the ability of a cancer cell to repair the DNA damage inflicted by the alkylating agent, specifically cisplatin (page 2446, first column, lines 37-40).

Liu et al teach a C242-DM1 conjugate (pages 170 to 171 in sections 2 and 3 Liu et al teach that the C242 maytansinoid conjugate killed antigen positive COLO 205 cells in vitro and caused decreased tumor burden of transplanted human colon cancer xenographs in immunodeficient mice.).

The abstract of Fiorentino et al teaches that clinical synergy is often evident in combinations with platinum (lines 5-8).

Schlom teaches that in all of the previous reported human trials in which non-immunosuppressed patients were treated with multiple doses of marine antibodies only the first and perhaps the second dose of said antibody was efficiently reaching the tumor site due to the HAMA response. Schlom teaches that it is unrealistic to assume that just one or two administrations of any anti-cancer therapeutic would be effective. Schlom teaches that the answer to this problem is the humanization of the marine antibodies (pages 97-98, bridging paragraph).

It would have been prima facie obvious at the time the claimed invention was made to combine a humanized C242-DM1 immunotoxin with cisplatin for treatment of patients with colorectal cancer. One of skill in the art would have been motivated to do so by the teachings of Lidor et al on the general mechanisms affording synergy with combinations of immunotoxins and alkylating agents and the further example provided by the synergistic interaction between the immunotoxin of Rosenblum et al (which is not related by antigen-binding or toxic moiety) and cisplatin. One of skill in the art would have a reasonable expectation that the combination with platinum would be synergistic as evidenced by the abstract of Fiorentino et al who cite platinum as an agent in clinical synergistic combinations.

One of skill in the art would be motivated to make the humanized version of the C242 antibody for administration of the maytansinoid immunoconjugate to humans. One of skill in the art would also be motivated to make the scFv fragment of the C242 for administration to humans based on the teachings of Liu et al regarding the poor penetration of immunoconjugates

Art Unit: 1642

into tumor (page 170, first column, lines 11-12) and the teachings of Schlom on the enhanced ability of scFv to penetrate tumor vasculature and the decreased HAMA response associated with antibody fragments. One of skill in the art would logically be motivated to make a reagent which would maximize the delivery of the maytansinoid to the tumor. By making a humanized C242 antibody, the lack of a HAMA response will allow more of the antibody to reach the tumor on subsequent doses. By making a scFv from C242 the smaller fragment will have a decreased HAMA response and better ability to penetrate into the tumor.

9. Claims 93-98, 100-111, 113, 115-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lidor et al and Chari et al or Rosenblum et al and Chari et al as applied to claims 93-97, 102-110, 115-120 above, and further in view of Liu et al (Proc Annu Meet Am Assoc Cancer Res, 1997, Vol. 38, page A190, cited in a previous Office action) and the abstract of Fiorentino et al (Dev Oncol, 1988, Vol. 54, pp. 415-435) and (Schlom (Monoclonal Antibodies: They're More and Less Than You Think, In: Molecular Foundations of Oncology, 1991, Ed. S. Broder, pp. 95-134)

The specific embodiments of claims 93-97, 101-110, 115-119 are set forth above. Claim 98 embodies the composition of claim 93 wherein the monoclonal antibody binds to a CD5 antigen. Claim 100 embodies the composition of claim 93 wherein the antibody or a fragment thereof is humanized N901. Claim 111 embodies the kit of claim 106 wherein the monoclonal antibody or a fragment thereof binds to CD56. Claim 113 embodies the kit of claim 106 wherein the monoclonal antibody or a fragment thereof is humanized N901.

The combinations of Lidor et al and Chari et al or Rosenblum et al and Chari et al do not specifically teach the combination of a humanized C242-DM1 conjugate. However, Lidor et al suggest the general property of synergism between an immunotoxin and cisplatin because Lidor et al proposes that the immunotoxin would decrease the ability of a cancer cell to repair the DNA damage inflicted by the alkylating agent, specifically cisplatin (page 2446, first column, lines 37-40).

Liu et al (AACR) teach that the administration an immunotoxin conjugate comprising the humanized N901 antibody and maytansinoid (DM1) was effective at killing human small cell lung xenographs in immunodeficient mice. The abstract of Lynch et al teaches that N901 is a

monoclonal antibody that binds to the CD56 neural cell adhesion molecule of NCAM., thus fulfilling the specific embodiment of claims 9 and 11 specifying binding to CD56. Liu et al do not teach the administration of cisplatin in conjunction with the immunotoxin.

The abstract of Fiorentino et al teaches that clinical synergy is often evident in combinations with platinum (lines 5-8).

Schlom teaches that in all of the previous reported human trials in which non-immunosuppressed patients were treated with multiple doses of marine antibodies only the first and perhaps the second dose of said antibody was efficiently reaching the tumor site due to the HAMA response. Schlom teaches that it is unrealistic to assume that just one or two administrations of any anti-cancer therapeutic would be effective. Schlom teaches that the answer to this problem is the humanization of the marine antibodies (pages 97-98, bridging paragraph).

It would have been prima facie obvious at the time the claimed invention was made to combine a humanized N901-DM1 immunotoxin with cisplatin for treatment of patients with small cell lung cancer. One of skill in the art would have been motivated to do so by the teachings of Lidor et al on the general mechanisms affording synergy with combinations of immunotoxins and alkylating agents and the further example provided by the synergistic interaction between the immunotoxin of Rosenblum et al (which is not related by antigen-binding or toxic moiety) and cisplatin. One of skill in the art would have a reasonable expectation that the combination with platinum would be synergistic as evidenced by the abstract of Fiorentino et al who cite platinum as an agent in clinical synergistic combinations. One of skill in the art would be motivated to make the humanized version of the N901 antibody for administration of the maytansinoid immunoconjugate to humans. One of skill in the art would also be motivated to make the scFv fragment of the N901 for administration to humans based on the teachings of Liu et al regarding the poor penetration of immunoconjugates into tumor (page 170, first column, lines 11-12) and the teachings of Schlom on the enhanced ability of scFv to penetrate tumor vasculature and the decreased HAMA response associated with antibody fragments. One of skill in the art would logically be motivated to make a reagent which would maximize the delivery of the maytansinoid to the tumor. By making a humanized N901 antibody, the lack of a HAMA response will allow more of the antibody to reach the tumor on

Art Unit: 1642

subsequent doses. By making a scFv from N901 the smaller fragment will have a decreased HAMA response and better ability to penetrate into the tumor.

10. Claims 93-97, 99, 102-110, 112, 115-119 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,208,020 in view of Lidor et al.

The specific embodiments of the claims are set forth above. Claims 1-6 of the '020 patent are drawn in part to cytotoxic agents comprising one or more maytansinoids conjugated to a monoclonal antibody or fragment thereof via a disulfide bridge at the C3 position of said maytansinoids and wherein said monoclonal antibody or fragment thereof is selective for tumor cell antigens. Claims 7-12 are drawn to pharmaceutical composition comprising maytansinoids conjugated to a monoclonal antibody or fragment thereof via a disulfide bridge at the C3 position of said maytansinoids and wherein said monoclonal antibody or fragment thereof is selective for tumor cell antigens. Conjugation of the monoclonal antibody to the maytansinoid via the C3 position of maytansinoid is the same as the structures of instant claims 102, 105 and 115-117.

Lidor et al teach a supra-additive cytotoxicity afforded by the combination of an immunotoxin and cisplatin (page 2443, first column, bridging sentence to second column). Lidor et al teach that immunotoxin modulate the sensitivity of ovarian cancer cells to alkylators and that the toxicity produced by immunotoxins operate by a mechanism which is distinct from alkylating agents, and thus the combination is advantageous for reasons of imparting to the cancerous cells two separate toxins (page 2446, first column, lines 32-40). Lidor et al teach that the toxin portion of the immunotoxin was ricin A chain (page 2440, first column, lines 11-12 under the heading of "Drugs and Immunoconjugates" and reference 9).

It would have been prima facie obvious to include cisplatin with the pharmaceutical compositions of claims 7-12. One of skill in the art would have been motivated to do so by the teachings of Lidor et al on the supra-additive toxicity afforded by the combination of an immunotoxin and an alkylating agent.

11. All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicant arguments.

Art Unit: 1642

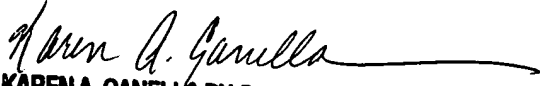
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

5/16/2005


KARENA CANELLA PH.D
PRIMARY EXAMINER